

INPLASY

Efficacy and safety of direct-acting antiviral agents (DAAs) in the treatment of patients with hepatitis C-related cirrhosis: a systematic review and Meta-analysis

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 June 2026 and was last updated on 29 June 2026.

INTRODUCTION

Review question / Objective To systematically assess the efficacy (SVR12 rate) and safety (AEs rate, SAEs rate, mortality rate) of direct-acting antiviral agents (DAAs) versus no unified comparative antiviral regimen in adult patients with hepatitis C-related cirrhosis, by synthesizing quantitative data from eligible published English studies.

Condition being studied Chronic hepatitis C virus infection-induced liver cirrhosis, which causes severe liver complications, increased adverse event risks and higher mortality during antiviral treatment.

METHODS

Participant or population Adult patients diagnosed with chronic hepatitis C-related liver cirrhosis; children, adolescents and patients complicated with other unqualified psychiatric/physical disorders are excluded.

Intervention Treatment with at least one type of direct-acting antiviral agent (DAAs), including sofosbuvir, velpatasvir, ledipasvir, daclatasvir, glecaprevir, pibrentasvir and combined DAA regimens.

Comparator No unified control intervention is set; all included studies adopt routine clinical observation without uniform comparative antiviral therapy as the baseline reference.

Study designs to be included Randomized controlled trials and non-randomized controlled trials/randomised controlled trials.

Eligibility criteria Inclusion criteria include: (1) Patients with chronic hepatitis C virus (HCV)-related cirrhosis. (2) Language: English. (3) Intervention measures: Treatment with at least one direct-acting antiviral agent (DAAs). (4) The outcome indicators should at least include one of the following items: ① Sustained virological response at 12 weeks after treatment (SVR12);

② Adverse events (AEs); Serious adverse events (SAEs); ④ mortality events.

Exclusion criteria are as follows: (1) Child or adolescent. (2) Conference abstracts, reviews, editorials, letters and other incomplete studies. (3) No studies reported outcome measures such as SVR12.

Information sources Four electronic databases: PubMed, Embase, Cochrane Library, Web of Science. Literature published from database inception to December 2025. Unreported data obtained by contacting original authors via email or telephone when necessary. No grey literature or trial registers searched.

Main outcome(s) Sustained virologic response at 12 weeks (SVR12): HCV RNA below quantification limit 12 weeks post DAA treatment discontinuation; pooled incidence rate with 95% CI.

Adverse events (AEs): Overall incidence of any adverse events during DAA treatment.

Serious adverse events (SAEs): Life-threatening, hospitalization-causing, disabling or fatal medical events during treatment.

All-cause mortality: Death events occurring during or after DAA therapy.

Quality assessment / Risk of bias analysis Cochrane Risk of Bias 2.0 (RoB 2.0) tool for RCTs, evaluating random sequence generation, allocation concealment, blinding, incomplete data, selective reporting and other bias (low/high/unclear risk). Newcastle–Ottawa Scale (NOS, total 9 points) for non-RCT cohort/retrospective studies: scores 7–9 = high quality, 4–6 = moderate, 0–3 = low. Disagreements resolved by a third researcher.

Strategy of data synthesis Stata 18 software for statistical analysis. All outcomes calculated as pooled incidence with 95% CI. I^2 and Chi-square test assess heterogeneity ($\alpha=0.1$). Fixed-effects model for low heterogeneity ($I^2<0.1$); random-effects model for high heterogeneity. Funnel plot, Egger's test and Begg's test to detect publication bias.

Subgroup analysis Subgroup stratification based on three moderators: 1) study design (RCT vs non-RCT); 2) study sample size; 3) multi-country vs single-country study scope. Q-test compares between-subgroup heterogeneity to explore sources of inter-study variance.

Sensitivity analysis Sensitivity analysis was performed to evaluate the stability of the summary results by excluding studies one by one. Each study was sequentially removed one by one, and a

meta-analysis was performed on the remaining studies at each stage, comparing the results with those before any studies were removed. There were no significant changes after the removal of the results. The sensitivity analysis indicated that the results were stable.

Country(ies) involved No unified specified countries; the included primary studies were conducted across multiple different countries worldwide.

Keywords Hepatitis C; Liver Cirrhosis; Treatment Efficacy; Safety; Antiviral Agents.

Contributions of each author

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